REMARKS

The First Rejection Under 35 USC § 112, first paragraph

The solvates of the compounds are cancelled from the claims, rendering the rejection moot.

The Objections Under 37 USC § 1.75

The claims are amended whereby it is clear that claims 3-4 are not substantial duplicates of claim 1.

The Second Rejection Under 35 USC § 112, first paragraph

All the allegations underlying the Office Action's rationale concern method aspects, yet the claims examined are directed to products, i.e., compounds and a pharmaceutical composition containing said compounds.

In sum, the Office Action appears to treat the product claims as if they were method claims directed to a variety of specific uses, i.e., various pharmaceutical applications. However, the product claims are not limited to any specified use as a method claim may be. As such, the rejection thereof as if they were method claims directed to a recited use is not justified. The products recited in the claims may be used for any purpose, including, e.g., the *in vitro* aspects taught in the specification or *in vivo* ones and others.

The Federal Circuit has specifically held that a product claim, i.e., a composition claim, cannot be read to embrace only certain uses because the composition claim would otherwise mutate into a method claim. See *Union Oil Co. of California v. Atlantic Richfield Co.*, 208 F.3d 989, 54 USPQ2d 1227 (Fed. Cir. 2000), wherein the Federal Circuit stated that "the '393 patent **claims compositions of matter. The scope of these composition claims cannot ... embrace only certain uses of that composition. ... Otherwise these composition claims would mutate into method claims**." (Emphasis added.)

Also important is to note the analysis used by the Federal Circuit in determining whether a pharmaceutical composition was enabled in *Amgen Inc. v. Hoechst Marion Roussel Inc.*, 65 USPQ2d 1385 (Fed. Cir. 2003). The inquiry exclusively focused on whether the individual components of a pharmaceutical composition were enabled and not on whether a particular use of said composition would be enabled. See the relevant part of the *Amgen* decision, which is reproduced below.

> Focusing specifically on the '422 patent, **the enablement inquiry** is whether Amgen has enabled all **pharmaceutical compositions** comprising "a therapeutically effective amount of human erythropoietin," "a pharmaceutically acceptable diluent, adjuvant or carrier," and human erythropoietin "purified from mammalian cells grown in culture." The court found that the specification described and enabled various possible diluents and carriers and provided specific information on effective dosages and therapeutic effect in mice. Id. at 148, 57 USPQ2d at 1506. Amgen also described and enabled at least one way of obtaining EPO purified from mammalian cells in culture: the genetic manipulation of CHO and COS-1 cells, followed by both described and other well known purification techniques. Finally, the court accepted testimony indicating that an ordinarily skilled artisan would infer from the COS-1 (monkey) and CHO cell examples that similar outcomes could be expected from other mammalian cells since all mammalian cells produce and secrete hormones like EPO by means of the same fundamental processes. Id. at 159, 57 USPQ2d at 1514-15. (Emphasis added.)

There is no basis for treating a product claim as if it was a method claim directed to particular use(s). As such, the rejections are improper and therefore should be withdrawn for at least this reason.

Although not necessary regarding the product claims, applicants address the specific allegations relevant to method claims as applicants are requesting the rejoinder of the withdrawn method claims upon allowance of the product claims, which should be allowable in view of the above as no outstanding rejections remain.

First and foremost, a specification disclosure which "contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support." (Emphasis added.) *In re Marzocchi*, 169 U.S.P.Q. 367, 369 (1971). "The PTO must have adequate support for its challenge to the credibility of applicant's statements of utility". (The quoted statement was made in the context of enablement, i.e., the how-to-use requirement of the first paragraph of section 112.) See also *In re Bundy*, 209 USPQ 48 (1981). The only relevant concern of the Patent Office should be over the truth of assertions relating to enablement. The first paragraph of section 112 requires

nothing more than objective enablement. See *In re Marzocchi, supra.*

The Office Action has not established any basis to doubt objective enablement. The Examiner has also provided no support for establishing that one of ordinary skill would doubt the objective truth of the asserted utility, which is enabled by the specification. The enablement rejection by the Office Action is thus unfounded. The rejection therefore was improper under *In re Marzocchi.*

The compounds of the claims are disclosed to have 5-HT_{2A} antagonistic activity, which in view of the state of the art is not objectively doubtable. Even the Office Action admits that compounds are known to have such activity and citation is made to several references. Moreover, the specification discloses a very large number of citations on pages 2-4 disclosing compounds with the recited activity and teaching the use thereof to a large variety of indications. Because other compounds are know with the disclosed activities in the art, there is no basis for the rejection as there is no indication that one of ordinary skill in the art would have questioned the effect of the drugs in view of the disclosure and the state of the art. See *Rasmusson v. Smithkline Beecham Co.*, 75 USPQ2d 1297 (Fed. Cir. 2005).

Despite the above admission and vast disclosure in the specification, the Office Action also alleges that there is no established nexus between the chemical structure of formula I and the treatment of certain diseases. See the top of page 5 o the Office Action. However, under the requisite standard of objective enablement, applicants have satisfied their burden.

The Office Action also alleges that there is no nexus between 5-HT_{2A} antagonistic activity and some diseases, including Parkinson's disease. In this regard, attached is Fernandez et al., Ariprazole for drug-induced psychosis in Parkinson disease: preliminary experience, Clin. Neuropharmacol. 2004 Jan-Feb; 27(1): 4-5, establishing a nexus between 5-HT_{2A} antagonist activity and Parkinson's disease.

The Office Action also notes that there are no data provided. However, there is no requirement for any examples or data in an application. See, for example, *Marzocchi*, supra, stating that "an enabling teaching is set forth, either by use of illustrative examples or by broad terminology, is of no importance." (Emphasis added.) The MPEP also agrees by stating that "compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, does not turn on whether an example is disclosed." (Emphasis added.) See MPEP § 2164.02.

Nevertheless, in this regard, attached is a declaration demonstrated that the seven compounds recited in claim 2 have remarkable activity on inhibiting the 5-HT_{2A} receptor.

Reference is also made in the declaration to the newly submitted reference by Fernandez et al., establishing a correlation before the filing of the present application of the 5-HT_{2A} receptor with Parkinson's disease.

Moreover, the Office Action alleges apparently regarding all the claims that they encompass a very large number of compounds. However, claim 2 recites seven specific compounds.

The Office Action also cites Wikipedia as the treatment of psychosis is correlated with 5-HT_{2A} receptor, but alleges that non-specific binding results in side effects and long term damage. Based on this, the Office Action appears to be requiring applicants to provide data on how the compounds can selectively bind the 5-HT_{2A}. However, whether side effects are present or not with the compounds (no admission of any sort made herein or implied), does not mean that they are not enabled for the treatment as recited in withdrawn claims. One of ordinary skill in the art faced with a variety of side effects in any case has various ways of dealing with such, e.g., modifying dosage amounts and/or routes and/or modes, diet of patient, etc., which are routine in the art. Moreover, it has long been established that the fact that a drug may exhibit some degree of toxicity or side effects does not provide a basis for refusal of patent. See, e.g., *In re Anthony*, 162 USPQ 594 (C.C.P.A. 1969) and *In re Sichert*, 196 USPQ 209 (C.C.P.A. 1977).

Yet the Office Action alleges that the specification does not provide guidance as to forming dosage in the effective yet non-toxic range for therapeutic use. There is no basis for this allegation. Applicants provide clear guidance regarding dosage amounts on page 11 of the application. Moreover, any allegation that such may be in the toxic range, for example, would be mere speculation by the Office Action, and as such cannot be used in the rejection where the standard is objective enablement.

In the pharmaceutical arts, relevant cases to the rejections herein is *In re Brana*, 51 F.3d 1560, 34 USPQ2d 1441 (Fed. Cir. 1995), where the Federal Circuit stated that

> usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful can be well before it is ready to be administered to humans. If the courts were to require Phase II testing in order to prove utility for pharmaceutical inventions, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer.

Applicants also point to *In re Bundy*, 642 F.2d 430, 209 USPQ 48, (CCPA 1981), where the disclosure only established the basic pharmacology for the compounds, but where no examples were provided. The specification stated that the compounds of the invention possess activity similar to E-type prostaglandins. Nevertheless it was found that sufficient guidelines as to use were given in the disclosure. The court held that "what is necessary to satisfy the how-to-use requirement of section 112 is the disclosure of some activity coupled with knowledge as to the use of this activity."

Reconsideration is respectfully and courteously requested.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

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